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Experience With Six Children With Fetal Rhabdomyomatous Nephroblastoma: Review of the Clinical, Biologic, and Pathologic Features

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Background. Fetal rhabdomyomatous nephroblastoma (FRN) is a rare variant of Wilms tumor.

Materials and Results. One hundred and thirty two children with kidney tumors were seen at our hospital from 1985 to 1993. Among them were 6 (4.5%) who had FRNs. Five were boys aged 8 months to 3 years; the girl was 17 months old. Three of the four with unilateral disease had tumors so large that they were considered unresectable at diagnosis. Five received pre-operative chemotherapy and three also received pre-operative radiation therapy. None of the tumors responded. Both patients with bilateral tumors died of progressive disease. Three of the four patients with unilateral disease followed for at least one year are alive for 1 to 10 years after diagnosis.

Conclusions. FRN should be in the differential diagnosis of huge kidney tumors in children, and preoperative therapies escalated with caution since FRN is not responsive to treatment used for classic Wilms tumor. Med. Pediatr. Oncol. 30:152-155, 1998.

Key words: Wilms tumor variants; kidney tumors; childhood cancer

INTRODUCTION

Most renal tumors in children are classic nephroblastomas but there are variant histology patterns that are associated with distinct morphologic, biologic and clinical features [1,2,3]. One of these variants is the fetal rhabdomyomatous nephroblastoma (FRN) [2]. It is characterized by less aggressive behavior, bilateral presentation in 30% of the cases, and the predominance of a fibrorhabdomyogenic component on histologic examination [2,4]. FRN histology is classified as an intermediate grade malignant pattern by the International Society of Pediatric Oncology [5].

MATERIALS AND METHODS

There were 132 cases of renal tumors referred to the Pediatric Department of the A.C. Camargo Hospital during the period 1985 to 1993. Six of them (4.5%) were classified as fetal rhabdomyomatous nephroblastoma.[†] The pathologic and clinical data of these patients were reviewed, and new sections were cut from stored, formalin-fixed paraffin-embedded tissue. These new sections were prepared with hematoxylin-eosin, Masson's trichrome and phosphotungsten hematoxylin stains.

RESULTS

Five of the 6 patients were boys. The ages of the six varied from 8 months to 3 years (median of 12 months). All patients were evaluated by physical examination, abdominal ultrasound, excretory urograms (IVP) and plain chest radiography. Two patients had bilateral renal tumors at diagnosis; another child with a unilateral tumor presented with pulmonary metastases. One of the six children underwent immediate nephrectomy; the others received pre-nephrectomy chemotherapy without previous biopsy (Table I). It included dactinomycin (2 cycles—60 mcg/kg in a single dose every 4 weeks) and vincristine (1.5/m^2/dose weekly for 4 to 6 weeks). Three of these 5 patients also received abdominal radiotherapy, and the child with pulmonary metastases was also given whole lung radiation therapy. No patient with a unilateral tumor had evidence of tumor shrinkage on follow-up diagnostic imaging. All of them underwent exploratory laparotomy with complete tumor excision without rupture. The tumors weighed 575 to 2080 grams, corresponding to 5–15% of the patients' body weights. The tumors were made up largely of rhabdomyomatous tissue (90–95%) with scattered foci of cartilaginous, smooth muscle and adipose tissue (Figure 1). It was not possible to make comparisons with the pre-treatment histology because none had had previous biopsy, but the tumor in the one patient who did not receive pre-operative chemotherapy had histology very similar to the others. Three

[†]One of these children was reported earlier by Saba et al. (see reference 7).

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TABLE I. Clinical Data

Case	Sex/Age (months)	Pre-operative treatment	Tumor weight	Outcome
1*	M/36	dactinomycin + doxorubicin + vincristine + RT**	1150 grs.	Alive— 10 years
2	F/17	dactinomycin + vincristine	Bilateral	Dead
3	M/15	none	575 grs	Alive— Lost to follow-up 1 year
4	M/11	dactinomycin + vincristine + RT**	1000 grs	Alive— Lost to follow-up 1 month
5	M/8	dactinomycin + vincristine	Bilateral	Dead
6	M/24	dactinomycin + vincristine	2080 grs	Alive— 2 years

*Reported previously. Ref. 7.
**RT = radiation therapy.

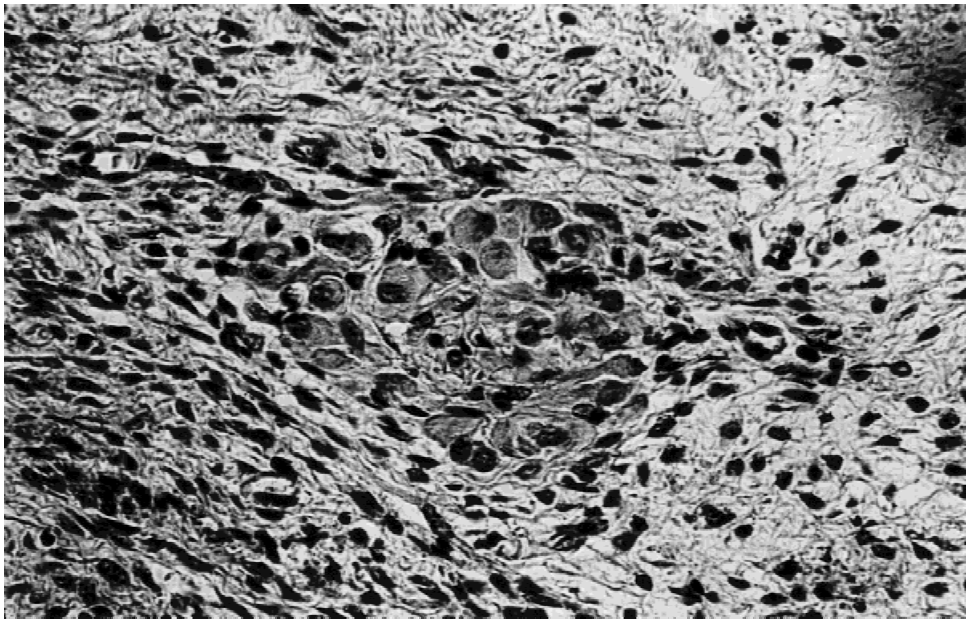

Fig. 1. Predominance of fetal rhabdomyomatous cells (H & E, ×20).

of these children are alive without disease from 1 to 10 years. The fourth was lost to follow-up without disease one month after surgery. Neither patient with bilateral renal tumors at diagnosis had evidence of tumor response on follow-up diagnostic imaging, and both died of progressive tumor growth.

DISCUSSION

Fetal rhabdomyomatous nephroblastoma (FRN) is considered to be a predominantly mesenchymal variant of Wilms tumor. It usually occurs in younger children, often is very large at diagnosis and both kidneys are affected in about one third of cases [2]. It does not seem to be a very aggressive lesion. Vicandi et al. [6] reported the incidence to be 2.1% in their experience; in our material, the frequency of FRN was slightly higher corresponding to 4.5%.

The predominant fibrorhabdomyomatous component of FRN is responsible for its rubbery consistency and fibromyomatous gross appearance, which was present on gross inspection of all 6 specimens. The pulmonary metastases present at diagnosis in one child showed multiple cystic spaces of various sizes separated from each other by necrotic and hemorrhagic areas. The pyelocalyceal system of the affected kidney in that child as well as the

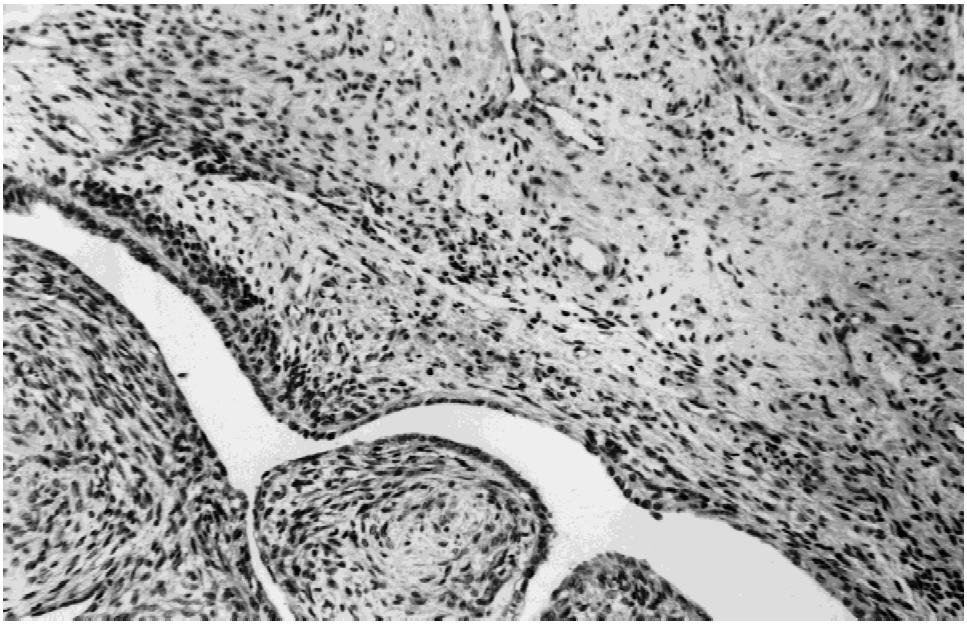

Fig. 2. A large polypoid projection into the pyelocalycial system (H & E, ×20).

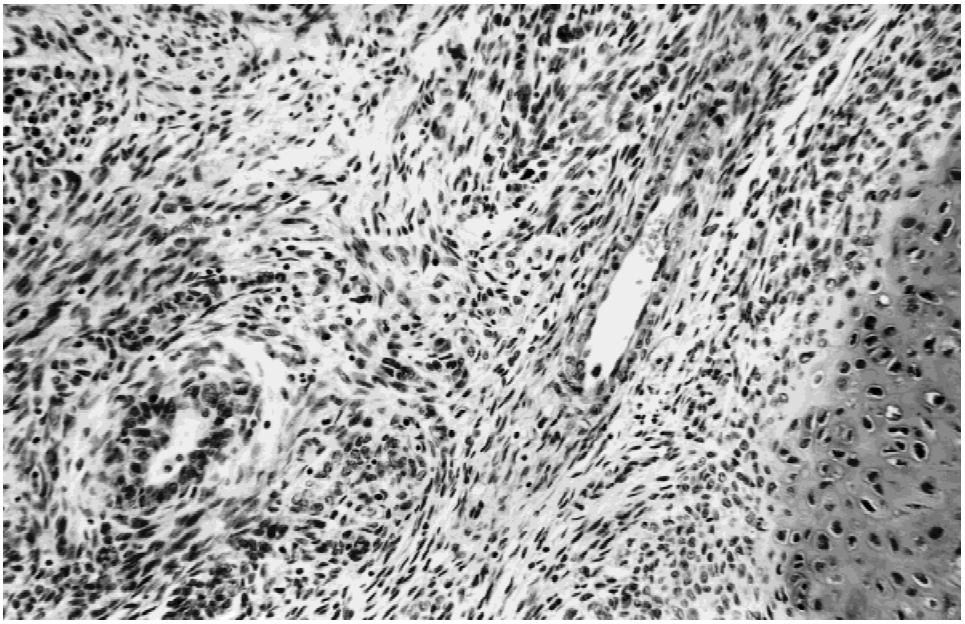

Fig. 3. Fibrous tissue around dilated tubule. A cartilaginous tissue focus is present on the right.

ureter showed whitish, rubbery polypoid projections (Figure 2). Mahoney et al. describe a similar case with the presence of a large intrapelvic polypoid mass grossly and histologically resembling sarcoma botryoides [8]. Histologically, the tumors in our patients were predominantly composed of skeletal muscle of fetal type with interspersed fibrous tissue involving dilated tubules lined by cuboidal epithelium (Figure 3). They also showed small foci of smooth muscle and cartilaginous and adipose tissue. In some areas there were small clusters of undifferentiated blastematous cells, sometimes with tubular differentiation. The paucity of neoplastic blastemal and epithelial elements and the extensive rhabdomyogenesis is thought to be the explanation for the less aggressive clinical behavior [2] and may also explain the poor response to adjuvant therapy [9]. None of our five patients showed significant tumor shrinkage after the preoperative treatments used, whereas in classic Wilms tumors, both preoperative chemotherapy and radiotherapy can be expected to do so [10,11].

It might be questioned whether the child with lung metastases at diagnosis could have had a typical Wilms tumor that was altered by preoperative therapy [7]. It is well known that preoperative irradiation can produce changes in the histologic patterns of Wilms tumor and lead to an increased proportion of striated muscle in the specimen [12]. Preoperative chemotherapy also modifies the microscopic features producing histologic changes such as reduction in the size of blastemal cells, necrosis, hemorrhage and an increase in foamy histiocytes and inflammatory cells.

Wilms tumor is a mixed tumor, with many histologic patterns. As therapy becomes more effective, it is important to determine which characteristics are associated with aggressiveness and which are associated with nonresponsiveness to therapy. Anaplasia is a marker of nonresponsiveness, while a diffuse blastemal pattern suggests aggressiveness [13]. FRN can also be associated with nonresponsiveness but with a different outlook, so that intensive therapy should be avoided.

CONCLUSION

The presence of a huge renal mass in a child does not necessarily indicate an ominous prognosis. FRN, which tends to be large at diagnosis and is not responsive to therapy, should be kept in mind, and preoperative therapy escalated in intensity only with caution when a childhood renal tumor fails to respond.

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